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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/016,752	10/30/2001	Ramy Lidor-Hadas	1662/55002	8981

26646 7590 04/20/2005

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EXAMINER	
OH, TAYLOR V	

ART UNIT	PAPER NUMBER
1625	

DATE MAILED: 04/20/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/016,752	LIDOR-HADAS ET AL.	
	Examiner	Art Unit	
	Taylor Victor Oh	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 January 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5-8,10-22,25-39,41,43,45-70 and 72-91* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5-8,10-22,25-39,41,43,45-70 and 72-91* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *30 October 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Final Rejection

The Status of Claims

Claims 5-8, 10-22, and 25-39, 41, 43, 45-70, and 72-91 are pending.

Claims 5-8, 10-22, and 25-39, 41, 43, 45-70, and 72-91 have been rejected.

Claim Objections

The objection of Claims 5-8 and 10-18 has been withdrawn due to the modification made in the amendment.

Claim Rejections - 35 USC 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The rejection of Claims 23, 40, 42, 44, 71, and 93 under 35 U.S.C. 112, first paragraph, has been withdrawn due to the cancellation of the claims; however, the rejection of Claims 89-91 under 35 U.S.C. 112, first paragraph, has been maintained because those claims still contain the phrase " pharmaceutically acceptable carrier"; therefore, the claims are considered to be the pharmaceutical composition.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The rejection of Claims 45, 66, and 92 are rejected under 35 U.S.C. 112, second paragraph, has been withdrawn due to the cancellation of claim 92; however, the rejection of Claims 45 and 66 has been maintained due to applicants' failure to modify the claims in the amendment.

Claims 10 and 16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims 10 and 16, the phrase " the ondansetron hydrochloride Form A containing between 5 % water and 10 % water" is recited. This expression is vague and indefinite because the term " containing " would imply that there are additional components besides the 5-10 % of water. Therefore, an appropriate correction is required.

Claim Rejections - 35 USC 102

The rejection of Claims 19-22, 49-50, 52, 57-58, 66-67, 74-76 under 35 U.S.C. 102(b) as being anticipated clearly by Wu Gousheng et al (CN 1113234).

The rejection of Claims 19-22, 49-50, 52, 57-58, 67, 74-76 under 35 U.S.C. 102(b) as being anticipated clearly by Wu Gousheng et al (CN 1113234) has been maintained due to applicants' failure to change the claim languages.

The rejection of Claims 23, 39-45, 62-65, 71, 87-91, and 93 under 35 U.S.C. 102(b) as being anticipated clearly by Wu Gousheng et al (CN 1113234) has been withdrawn due to applicants' persuasive argument and the cancellation of the claims .

Claim Rejections - 35 USC 103

1. Applicants' argument filed 1/27/05 have been fully considered but are persuasive.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The rejection of Claims 5-8, 10-22, and 25-39, 41, 43, 45-70, and 72-91 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wu Gousheng et al (CN 1113234).

The rejection of Claims 5-8, 10-22, and 25-39, 41, 43, 45-70, and 72-91 under 35 U.S.C. 103(a) as being unpatentable over Wu Gousheng et al (CN 1113234) is maintained for the reasons of the record on 7/28/04.

Applicants' Argument

Applicants argue the following issues:

1. with respect to claims 19-23 and 39-45, the teachings of the Wu Gousheng reference does not describe an anhydrous form ;

2. with respect to claims 49-50, 52,57-58 , 66-67, 74-76 and 93, the Wu Gousheng reference does not disclose any of the claimed polymorphic forms;

3. with respect to claims 62-66, the Wu Gousheng reference does not disclose an isopropanolate form;

4. with respect to claims 87-91, the Wu Gousheng reference is silent regarding particle size;

5. with respect to claims 5-7, the Wu Gousheng reference does not suggest the use of a mixture of ethanol and water ;

6. with respect to claim 8, the Wu Gousheng reference does not suggest hydrating the monohydrate under 50 % relative humidity;

7. with respect to claims 10-18, the Wu Gousheng reference does not suggest a product having an intermediate degree of hydration nor any process of making such a product;

8. with respect to claims 25-38, 39, 41, 43,45, 46-48, 51, 53-56, 59-65, 68-70, and 72-86, the Wu Gousheng reference does not suggest any of these polymorphs , nor any process of preparing them;

9. the Wu Gousheng reference does not suggest the use of particular claimed solvent systems, toluene, xylene, ether, etc. ; therefore, they serve different functionality.

Applicants' arguments have been noted, but the arguments are not persuasive.

First, regarding the first and second arguments , the Examiner has noted applicants' arguments. However, the Wu Gousheng reference does indicate that there is a teaching of forming ondansetron hydrochloride monohydrate by using ondansetron hydrochloride dihydrate compound under a certain reaction condition. The Claims are product claims, in which applicants recite some of the physical and chemical characteristics of the said product. MPEP 2112 says:

"SOMETHING WHICH IS OLD DOES NOT BECOME PATENTABLE UPON THE DISCOVERY OF A NEW PROPERTY

The claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. In re Best, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977)."

In this case, the "unknown property" is the particular crystalline form with X-ray diffraction pattern and with Infra Red (IR) spectra containing peaks. This is unknown because the reference is silent on this property. MPEP 2112 goes on to state:

"A REJECTION UNDER 35 U.S.C. 102/103 CAN BE MADE WHEN THE PRIOR ART PRODUCT SEEMS TO BE IDENTICAL EXCEPT THAT THE PRIOR ART IS SILENT AS TO AN INHERENT CHARACTERISTIC

Where applicant claims a compound in terms of a function, property or characteristic and the compound of the prior art is the same as that of the claim but the function is not explicitly disclosed by the reference, the examiner may make a rejection under both 35 U.S.C. 102 and 103, expressed as a 102/103 rejection."

Again, the "CHARACTERISTIC" which the prior art is silent on is the anhydrous crystalline form.

This is not an ordinary inherency situation where it is not explicitly stated what the product actually is. Here the reference explicitly teaches exactly what the compound is. The only difference is a characteristic about which the reference happens to be silent. See also Ex parte Anderson, 21 USPQ 2nd 1241 at 1251.

Applicants are reminded that the PTO has no testing facilities. If applicants' reasoning were accepted, then any anticipation rejection of an old compound could always be overcome by tacking on some characteristic or property which the reference was silent on, regardless of whether the prior art material was any different from the claimed material.

Note that the prior art compound has the following data: IR, MS, HNMR, CNMR, and melting point. Applicant's disclosure has none of these data, but instead it discloses thermogravimetric analysis and X-ray powder diffraction data. Applicants can overcome the 102(b) rejection, by showing that their anhydrous crystalline form and polymorphs of Ondansetron is different from the prior. Furthermore, it is not uncommon to find several polymorphs of compounds existing under normal handling conditions.

Just as every polymorph has its own characteristic X-ray patterns, so does every solvate. Therefore, the prior art still reads on the product claims.

Second, regarding the third argument , the Examiner has noted applicants' arguments. However, one among the various alcohols, isopropanol, is a well-known alcohol in the art. The Wu Gousheng reference does teach the use of n-propanol on page 11 (embodiment C_2), which is a structural isomer to isopropanol, similar to the functionality of the claimed solvent. Furthermore, the prior art has offered guidance that the use of water-alcohol solvent is possible in the preparation of Ondansetron hydrochloride (page 2 , lines 29-34). Therefore, it would have been obvious to the skilled artisan in the art to be motivated to employ the known isopropanol as an alternative to the structurally similar isomer of n-propanol in order to make the isopropanolate form of Ondansetron. This is because the skilled artisan in the art would expect such a modification to be successful as the guidance(page 2 , lines 29-34) shown in the prior art. Therefore, the reference is still relevant and applicable to the rejection of the claimed invention.

Third, regarding the fourth argument , the Examiner has noted applicants' arguments. However, concerning the particle size , the limitation of a process with respect to ranges of pH, time and particle size does not impart patentability to a process when such values are those which would be determined by one of ordinary skill in the art in achieving optimum operation of the process. Particle size is well understood by those of ordinary skill in

the art to be a result-effective variable , especially when attempting to control selectivity of the intended process.

Fourth, regarding the fifth argument , the Examiner has noted applicants' arguments. However, concerning the use of the mixture of ethanol and water , the prior art has offered guidance that the use of water-alcohol solvent is possible in the preparation of Ondansetron hydrochloride (page 2 , lines 29-34). Furthermore, in particularly, Embodiment C_4 (see page 12) does use ethyl alcohol in conjunction with water in the preparation of Ondansetron hydrochloride. The reference is still relevant to the claimed invention.

Fifth, regarding the sixth and seventh arguments , the Examiner has noted applicants' arguments. However, concerning the use of the 50 % relative humidity and making an intermediate degree of hydration, the prior art has offered guidance that the final product is rinsed with water in the preparation of Ondansetron hydrochloride (see page 11, Embodiment C); therefore, it possible for the skilled artisan to adjust the exposure of water to the final product depending on the artisan' desirability of increasing water content in the final product. Moreover, the limitation of a process with respect to ranges of pH, time and concentration does not impart patentability to a process when such values are those which would be determined by one of ordinary skill in the art in achieving optimum operation of the process. Concentration is well understood by those of ordinary skill in

the art to be a result-effective variable , especially when attempting to control selectivity of the intended process. The reference is still relevant to the claimed invention.

Sixth, regarding the eighth and ninth arguments, the Examiner has noted applicants' arguments. However, concerning the use of making polymorphs and the use of various solvent, it is not uncommon to find several polymorphs of compounds existing under normal handling conditions. the Wu Gousheng reference does teach the use of various solvents, such as benzene and n-propanol, methyl alcohol, and ethyl acetate in the preparation of Ondansetron hydrochloride; therefore, it's quite possible to produce various polymorphs. Furthermore, particular claimed solvent systems such as , toluene, xylene, ether, are well-known solvents in the art, which have a similar functionality as the prior art'solvents. Therefore, there is no patentable weight over the prior art reference in the absence of an unexpected result using the claimed solvent system.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Taylor Victor Oh whose telephone number is 571-272-0689. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Tsang Cecilia can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

*** 4/16/15

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